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FURTHER STUDIES ON THE INFLUENZA EPIDEMIC AT CAMP GRANT

EDWIN F. HIRSCH AND MARION MCKINNEY

From the Laboratory of the Base Hospital, Camp Grant, Ill.

The epidemic of influenza at Camp Grant reached its decline by Oct. 18, 1918, but for some time afterward the death rate in the hospital from respiratory diseases or their complications continued to be high. As similar epidemics had been, and at that time were, rampant in many camps and civil communities, it seemed important to continue the studies instituted during the epidemic. Such an investigation would throw light on the bacteriology of any subsequent recrudescence of acute respiratory infections in a military camp after an influenza epidemic with bronchopneumonia. Due regard must be taken of the transient stay of the soldiers in this camp soon after the armistice, Nov. 11, 1918, and while patients were admitted to the hospital with the clinical diagnosis of influenza, only during the few weeks after the epidemic proper were the clinical course and the severity of symptoms the same as in patients admitted during the main epidemic.

Starting in December and continued into March of this year, 455 throat cultures of patients admitted for influenza were studied on plain blood agar according to the methods used earlier.

TABLE 1

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RESULTS OF STUDY OF THROAT CULTURES OF INFLUENZA	Patients
Gram-positive, lancet-shaped diplococci, some- times in chains, growing in green colonies	
on plain blood agar in	71.87%
Hemolytic streptococci	21.98%
Nonhemolytic streptococci	9.01%
B. influenzae	19.58%
M. catarrhalis	72.31%

Of the gram-positive, lancet-shaped diplococci, 169 pure cultures were isolated and studied more carefully; 19 were soluble in bile and fermented inulin, 43 were soluble in bile only, 45 fermented inulin only, and 32 gave no reaction with either of these tests.

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¹ Hirsch and McKinney: Epidemic of Pneumococcus Bronchopneumonia, Jour. Infect. Dis., 1919, 24, p. 594.

The anatomic changes observed after death, when the epidemic had subsided, were chiefly such as complicate or follow pneumonia. Empyema was the commonest, usually in patients in whom the purulent exudate in the chest had been drained. Acute suppurative pneumonia with multiple peribronchial abscesses without definite limiting membranes was fairly common. The amount of destruction in such lungs varied widely, in some practically all the respiratory tissue of a lobe Hemolytic streptococci were or a lung having been destroyed. recovered from the exudate of such lungs with great regularity. It is possible that all of these acute suppurative pneumonias were essentially such from the beginning, but there is reason for believing that some of them were superimposed on a primary pneumonia without suppuration, because the examination of sections from earlier stages of such lungs showed necrosis in the alveolar walls or ductuli alveolares, this necrosis being but a small part of a much larger consolidation with changes like those in pneumococcus infection. In addition acute suppurative leptomeningitis and acute thrombo-ulcerative endocarditis were observed a few times.

Much different were the results in deaths from acute respiratory infections that in no way could be considered a complication of the epidemic disease. This group contains the largest number. Here the lungs were mottled by many, comparatively small, dark red areas, the increased firmness being due largely to the escape of blood into the substance. Large amounts of bloody fluid escaped from the cut surfaces, and the pleural cavities contained from 100 to 500 cc of thin reddish-brown fluid. Hemolytic streptococci were recovered in pure culture from the lungs and heart blood. In other cases the lungs contained irregular, nodular consolidations several centimeters in dimension, representing an older stage, and culturally yielding a similar bacterial flora. These nodules do not resemble in close detail the consolidations observed during the height of the epidemic in that the surfaces of the latter at the same stage of development were more coarsely granular without the yellow focal areas of necrosis, and the fluid expressed from the tissues was more viscid and grayish-brown rather than the reddish-brown of hemolytic streptococcus infection. The early acute hemolytic streptococcus pneumonia is also quite distinctive from the pneumonia of the epidemic.

During the 5 months in which these observations were made, there were only three cases in which the typical lobar pneumonia was

approached. All of these were noted after March 15, 1919. Consolidations of entire or nearly entire lobes were observed, but these were confluent bronchopneumonia rather than lobar pneumonia. That lobar pneumonia should be submerged during the epidemic and for months after, is of great interest. There seems to have been some fundamental change in the reaction of the host toward the infecting agent, some difference in the activity of the invading organism, or change in the interaction of both. Having found the pneumococci recovered during the epidemic highly virulent in resistant animals, might not absence of typical lobar pneumonia be explained on the basis of heightened virulence?

Cultures of tissues and fluids taken postmortem afford valuable information in acute infectious diseases of the variety of pathogenic bacteria present, and correlate the lesions with the organism concerned. The methods used during the epidemic were continued with slight modification in this study. As a rule, the cultures were obtained within 6 hours after death, and usually were controlled by direct smears made at the same time, stained later by Gram's method and dilute aqueous fuchsin.

During the period when complications of pneumonia were observed postmortem, and again later in a number of acute respiratory infections, hemolytic streptococci were recovered in mixed and pure cultures. With the ascendence of hemolytic streptococci in cultures, pneumococci became less frequent, although there were a few examinations during the first 3 months in which the lung changes and results of cultures corresponded well with those of the epidemic. In all the cultures from various places, influenza bacilli were found only occasionally with other organisms, never in pure culture. Pure cultures of staphylococcus albus were recovered from diseased lung tissues, body fluids, and the spleen in two examinations.

The lung culture results are briefly as follows for 49 of the 89 cases studied in which death probably had resulted from an acute respiratory disease after the epidemic or from lung complications of the epidemic disease:

TABLE 2 Lung Culture Results

30
20
11
8
2

This tabulation may be misleading in that each of the various organisms listed as being present was not regarded in every instance as being the predominant organism. Of the remaining 40 examinations, 31 presented no immediate reason for culture of the lung, 3 others were not tabulated because of an active tuberculosis, while in the remaining 7 an acute suppurative leptomeningitis was demonstrated, the spinal fluid of 4 containing pneumococci, and of 3 hemolytic streptococci.

TABLE 3

RESULTS OF THE HEART BLOOD CULTURES OF THE EIGHTY-NINE NE	CROPSIES
Hemolytic streptococcus, pure	26
Pneumococcus, pure	18
Staphylococcus albus, pure	2
Negative	16
NT-4144	27

These results indicate that with the decline of the epidemic and subsequently, hemolytic streptococci became important as invaders of tissues already diseased, and frequently provoked disease in tissues not the site of a preceding change.

The postmortem bacteriologic studies demonstrated the presence of hemolytic streptococci, pneumococci and staphylococci in diseased fluids and tissues. Many strains were inoculated intraperitoneally into white mice in measured fractional quantities of 24-hour blood-agar slant cultures according to methods given in the previous report. With the technic used, the results from testing 51 strains of hemolytic streptococci, 48 strains of pneumococci, and 4 strains of staphylococcus albus indicate that the white mouse is more susceptible to the pneumococcus than to either of the other two organisms. Very few strains of hemolytic streptococci and none of the staphylococci killed white mice in quantities smaller than 0.166 c c of a 24-hour blood-agar slant culture, while many strains of pneumococci killed mice in quantities as small as 0.00154 of a culture.

As the virulence of certain of the epidemic strains of pneumococci had been tested in rabbits and guinea-pigs, similar tests were made with strains recovered postmortem after the epidemic from diseased lungs that approached more nearly lobar pneumonia.

Lung Culture.—Pneumococcus type 2 bile soluble, fermented inulin, capsulated, injected intraperitoneally into three guinea-pigs in respectively $\frac{1}{4}$, $\frac{1}{2}$ and 1-24 hour blood agar slant culture amounts. Two pigs died ($\frac{1}{2}$ and 1 culture); four rabbits were given intravenously $\frac{1}{4}$, $\frac{1}{2}$, 1 and 2-24 cultures; all lived but the one given 2 slant cultures.

Heart blood culture from same necropsy with identical characteristics were injected as above into three guinea-pigs, killing them all, and into three rabbits in ½, 1, and 1-24 hour culture, killing one rabbit (1-24 hour culture); organism recovered pure from dead animals.

Similar experiments were made with four strains of pneumococci recovered postmortem April 8, 1919, each one, type 4, bile soluble, capsulated, fermented inulin and killed mice in dilutions as high as 0.0000154-24-hour blood-agar slant culture.

Three guinea-pigs and three rabbits were given as in the previous experiments $\frac{1}{4}$, $\frac{1}{2}$ and 1-24 hour blood-agar slant culture of each strain. All lived except two pigs receiving $\frac{1}{4}$ and 1-24-hour slant culture of different strains; organisms recovered pure from dead animals.

Rabbits and guinea-pigs receiving 0.1-24-hour blood agar slant culture of the epidemic strains died within a very short time, but a full 24-hour blood-agar slant culture of strains recovered from lungs postmortem with gray consolidations of lobar pneumonia since the epidemic failed constantly to kill such animals.

During, and especially with and after, the decline of the epidemic, hemolytic streptococci were recovered from diseased tissues and blood fluids. Of strains recovered from various places, 79 were classified according to their ability to ferment lactose, mannite, and salicin as suggested by Holman.² All but 8 of these strains fermented lactose and salicin, but did not ferment mannite. None of the strains fermented inulin or were soluble in bile.

SUMMARY

With the decline of the influenza epidemic at Camp Grant, the changes noted at postmortem examinations were chiefly such as occur with a healing or complicated pneumonia.

The postepidemic pneumonias differed from the epidemic in that changes commonly recognized as due to hemolytic streptococcus were frequent.

Occasionally the epidemic type of pneumonia was noted within three months after the epidemic, but more recently the classical gray lobar variety was observed.

The postmortem bacteriologic studies demonstrated a high incidence of hemolytic streptococcus infections, less frequently pneumococcus.

The virulence of pneumococci recovered from diseased lungs since the epidemic is less in rabbits and guinea-pigs than the epidemic strains.

Hemolytic streptococci recovered during and since the epidemic, according to Holman's classification belong chiefly to the pyogenes group.

² Jour. Med. Research, 1916, 34, p. 377.